THE SUPPOSED RELATION BETWEEN PARALYSIS AGITANS AND INSUFFICIENCY OF THE PARATHYROID GLANDS.

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Lundberg[1] in 1904 and Berkeley[2] in 1905 suggested that parathyroid insufficiency may be responsible for the symptoms of paralysis agitans. That these symptoms in many ways resemble those observed after removal of the parathyroids in lower animals is true, but attempts at establishing a close relationship between the two have not been successful. Examination of the parathyroids removed from cases of paralysis agitans at autopsy has revealed no characteristic deviation from the normal.[3] Berkeley[4] lays great stress upon the results he has obtained in the treatment of paralysis agitans with parathyroid preparations. Others,[5] however, have not observed favorable results from such treatment. Roussy and Clunet,[6] indeed, claim that the administration of parathyroid to their patients increased the severity of the symptoms. They also report finding hyperplastic parathyroids at autopsy, and come to the conclusion that hypertrophy of the parathyroid is an important factor in the etiology of paralysis agitans. This view is exactly contrary to that of Lundberg and Berkeley.

It seemed desirable to attack the subject from another direction, indicated by the results of the author's experiments upon dogs.[7] These have shown that after parathyroidectomy there is a marked diminution in the excretion of phosphorus. This persists until tetany appears and even longer. Analyses of the blood and serum of parathyroidectomized dogs show a decided increase in the content of phosphorus above the normal. This is due almost entirely to an increase in those phosphorus compounds that are not soluble in acetone, alcohol, or ether, but which are soluble in a mixture of dilute hydrochloric or acetic acid, and picric acid. This increase can readily be demonstrated before marked tetany has developed.

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[1] Deut. Zeitschr. f. Nervenheilkunde, 1904, xxvii, p. 217.

[2] Med. News, 1905, lxxxvii, p. 1000.

[3] Thompson, Jour. Med. Res., 1906, x. p. 399; Erdheim, Mitt. Grens. d. Med. u. Chir. 1906, xvi. p. 731; Berkeley, Presbyterian Hospital Reports, 1906, p. 170; Camp. Jour. Amer. Med. Assoc., 1907, xlviii, p. 1230; Alquier, Gaz. des Hôp., 1909, lxxxii, p. 1653; Gjestland, Zeitschr. klin. Med., 1912, lxxvi, p. 237; Haberfeld, Marañon, cited in Biedl, Inn. Sekretion, 1913, 2d. ed., p. 107.

[4] Internat. Clinics, 1912, series 22, vol. iv.

[5] Parhon and Golstein, Les Sécrétions internes, 1909, cited by Morel, Les Parathyroides, 1912, p. 292.

[6] Arch. méd. exp., 1910, xxii, p. 402.

[7] Greenwald, Amer. Jour. Physiol., 1911, xxviii, p. 103; Jour. Biol. Chem., 1913, xiv, pp. 363 and 369.

If parathyroid insufficiency is a factor in the etiology of paralysis agitans, it is probable that a similar increase in the amount of acid-soluble phosphorus would be found in the blood-serum of patients with paralysis agitans. It was therefore determined to apply the above test to the study of human serum. Since data concerning the lipoid-phosphorus content of human serum are not very extensive, this was also estimated. The results are therefore included in the table, although they are not relevant to the question under discussion.

The patients were selected by Dr. S. Wachsmann, medical director of the Montefiore Home, and the blood was drawn by Dr. H. Smith, to both of whom I am greatly indebted for their coöperation.

On the morning the blood was to be taken the patients received no food. In this way variations due to the character of the food and the stage of absorption were avoided. At about ten o'clock, or sixteen hours after the last meal, the blood was drawn from one of the veins of the forearm into sterile test-tubes and allowed to clot. The next day the serum was poured off and freed of cells by centrifuging. The absolutely clear and hemoglobin-free serum, generally about 50 gm., was weighed in a 700 c.c. Erlenmeyer flask and treated with at least four times its weight of acetone. This served to precipitate all the protein and the inorganic phosphate, leaving only the lipoid phosphorus in solution. It is important that the serum be clear and free from hemoglobin, as otherwise it contains enough inorganic phosphate derived from the erythrocytes to vitiate the analyses.

After standing at least six hours the mixture was poured into a wide glass tube, on the lower end of which was tied a piece of fine linen cloth, which acted as a filter. The filtrate was collected in a flask. The precipitate was rinsed into the tube with acetone and allowed to drain for several hours. It was then extracted with hot acetone in a continuous extraction apparatus for eight hours. The extract was added to the aqueous acetone filtrate previously obtained. The acetone was distilled off and the phosphorus determined by Bang's[8] modification of the Neumann method.[9] The residue in the tube was dried, ground to a fine powder, and extracted with absolute alcohol and anhydrous ether for four hours each. The extracts were combined, the solvents distilled off, and the phosphorus in the residue determined. The amount was negligible. The residue was dried, powdered, and returned to the flask in which the precipitation had previously been performed, and there treated with 500 c.c. of a solution containing 1 per cent. of concentrated hydrochloric acid and saturated with picric acid. The dilute hydrochloric acid dissolved all the inorganic phosphate, and the picric acid prevented the swelling of the protein. The mixture was shaken frequently, and, after at least sixteen hours, was filtered. After noting the volume of the filtrate, it was used for a determination of the phosphorus. The results were calculated to the original volume of 500 c.c. The residue, including the filter-paper, was also oxidized and the phosphorus determined. The amount was negligible, being approximately what was contained in the volume of liquid adhering to the protein and filter paper. That the method gives good results is demonstrated by the experiments previously reported.

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[8] Biochem. Zeitschr., 1911, xxxii, p. 443.

[9] Zeitschr. physiol. Chem., 1903, xxxvii, p. 115.

As has already been explained, if the symptoms of paralysis agitans are due to parathyroid insufficiency, we may expect to find that the amount of acid-soluble phosphorus in the blood serum of such patients is greater than in that of other individuals. As is evident from the table, this is not the case. These results, therefore, do not support the view that parathyroid insufficiency plays a role in the etiology of paralysis agitans.

CONTENT OF PHOSPHORUS IN HUMAN SERUM. MILLIGRAMS OF PHOSPHORUS PER KILO OF SERUM.

Name.	Diagnosis.	Acetone extract.	Acid extract.
J. M.	Paralysis agitans	123.0	39.7
C. W.	Paralysis agitans	106.8	29.6
F. S.	Paralysis agitans	57.8	32.1
N. S.	Paralysis agitans	90.5	43.9
H. F.	Paralysis agitans	83.2	35.0
D. R.	Paralysis agitans	83.6	49.2
W. W.	Paralysis agitans	96.2	37.3
M. H.	Normal	135.3	37.4
		134.7	34.2
L. S.	Hysteria	101.3	34.5
R.	Paraplegia, hysteria, cystitis	99.6	24.3
H. G.	Endarteritis	109.9	43.2
F. K.	Cataract, glaucoma	128.0	45.4
M. W.	Multiple sclerosis	81.6	36.9
J. H.	Multiple sclerosis	117.3	47.2
		113.8	47.3
E. D.	Multiple sclerosis	74.9	34.9
J. C.	Tabes	83.7	38.3
M. N.	Tabes	99.1	40.5
		90.7	42.4
H. S.	Hemiplegia	125.0	38.2